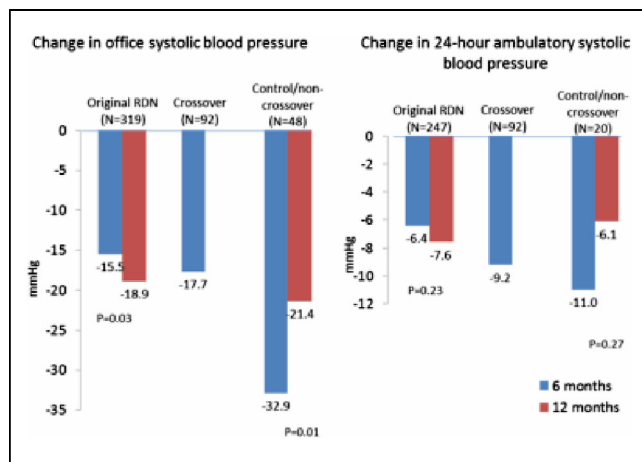


**RESULTS** The pattern of change from baseline to 6 months and 6 to 12 months following unblinding showed a decrease of BP in the RDN arms over time and an increase in BP in the control/non-crossover arm from 6 to 12 months as assessed by both office and ambulatory BP (Figure). Outcomes at 24 months, including office and ambulatory BP, available at TCT 2015, will be important to assess whether this pattern is maintained. Long-term safety will also be presented.

**CONCLUSIONS** The office systolic BP reduction in the RDN arm continued to increase between 6 and 12 months while the opposite relationship existed in the non-crossover patients. Outcomes at 24 months of unblinded treated subjects and non-treated control subjects will provide new insights to guide our continued understanding of the effects of patient selection, medication burden, and medication adherence in patients with treatment-resistant hypertension as well as confirm long-term safety in this large population treated with RDN.



**CATEGORIES ENDOVASCULAR:** Hypertension Therapies and Renal Denervation

**KEYWORDS** Renal denervation

#### TCT-84

##### Enhanced Circumferential Ablation using a Multi-electrode Bipolar/Unipolar Over-the-Wire Renal Denervation RF Catheter System with Closed Loop Sensing

Abraham R. Tzafri<sup>1</sup>, Lynn Bailey<sup>2</sup>, John Keating<sup>2</sup>, Fernando Garcia-Polite<sup>2</sup>, Peter Markham<sup>1</sup>, David Prutchi<sup>3</sup>, Elazer R. Edelman<sup>4</sup>

<sup>1</sup>CBSET Inc., Lexington, MA; <sup>2</sup>CBSET, Inc., Lexington, MA; <sup>3</sup>Renal Dynamics, Mount Laurel, NJ; <sup>4</sup>Harvard-MIT Biomedical Engineering Center, Cambridge, Massachusetts

**BACKGROUND** Posthoc analysis of SYMPPLICITY HTN-3 has revealed a trend for greater blood pressure reductions with increasing number of ablations and highlighted the difficulty of achieving uniform and circumferential ablation pattern using single electrode renal denervation catheters. We examined whether iterative low power multi-electrode bipolar-unipolar treatments based on local closed-loop temperature sensing can provide effective four quadrant ablations.

**METHODS** Ten porcine renal arteries were treated once (n=4) proximally or twice in sequence (n=6) ~6mm distal to the aortic ostium of the renal artery using the ReDy™ system with a 72°C set point (1.1±0.5 W, n=10). A low profile, 9-electrode, over-the-wire, RF 'basket' catheter with closed loop temperature control, and a smart generator delivers a 60sec sequence of bipolar and unipolar treatments designed to ensure that each electrode meets a temperature-duration objective. Catheters were advanced into the renal artery and positioned for treatment using a 6-Fr guiding sheath under fluoroscopic guidance. In the dual treatment group the catheter was retracted half a basket length after the first treatment. At 7 days post treatment, kidneys were harvested for norepinephrine (NEPI) quantification and arteries processed for histopathology. Post treatment NEPI levels were evaluated relative to our published baseline levels (666±222 ng/g, n=12) to calculate percent reductions. Automated image processing of H&E

stained tissue sections estimated the percentage of affected circumference up to a depth of 5 mm from the lumen.

**RESULTS** There was no angiographic evidence of acute dissection, perforation, or occlusion at the time of the procedure or subsequently. Histologically all treated arterial sections exhibited advanced re-endothelialization, with progressive arterial and peri-arterial repair, and no evidence of adverse effects on arteries or surrounding tissue. Summation of ablation effects over multiple tissue sections revealed that a larger percentage of the total circumferential arc was affected by dual treatments compared to single treatments up to 3 mm from the lumen. The difference between single and dual treatments was particularly pronounced up to 1 mm away from the lumen, 53.5±31.6% vs 87.5±11.2% (p=0.11) and appeared to predict relative NEPI reduction, 60.6±38.5% (p=0.03) vs 88.1±17.0% drop (p<0.001).

**CONCLUSIONS** We and others have argued for distal treatments based on the relative accessibility of target nerves, yet such treatments carry greater risk of affecting surrounding organs, particularly close to the hilus. The data herein illustrate that low power dual distal treatments using the Renal Dynamics ReDy™ system provide effective circumferential ablation without affecting arterial patency or surrounding organs.

**CATEGORIES ENDOVASCULAR:** Hypertension Therapies and Renal Denervation

**KEYWORDS** Ablation, radiofrequency, Histopathologic examination, In Vivo

#### TCT-85

##### Safety and Performance of the EnligHTN Renal Denervation System in Patients with Severe Uncontrolled Hypertension: 12 Month Results from the EnligHTN II Study

Melvin Lobo,<sup>1</sup> Joseph Montarello,<sup>2</sup> Manish Saxena,<sup>3</sup> Ajay Jain,<sup>4</sup> Darren Walters,<sup>5</sup> Matthew W. Pincus,<sup>6</sup> Stephen G. Worthley<sup>7</sup>  
<sup>1</sup>William Harvey Research Institute, London, United Kingdom; <sup>2</sup>Royal Adelaide Hospital, Adelaide, Australia; <sup>3</sup>BartsHealth NHS Trust, London, UK; <sup>4</sup>Barts Health NHS Trust, London, United Kingdom; <sup>5</sup>Prince Charles Hospital, Brisbane, Brisbane, Qld; <sup>6</sup>The Prince Charles Hospital, Chermisia, Queensland; <sup>7</sup>The University of Adelaide, Adelaide, Australia

**BACKGROUND** Percutaneous sympathetic renal artery denervation is available for the treatment of patients with resistant hypertension. We further investigated the safety and efficacy of a multi-electrode renal denervation system (EnligHTN™) in patients with severe uncontrolled hypertension.

**METHODS** The EnligHTN-II study is a post-market clinical investigation in which patients were assigned to one of three groups; Group A, office systolic BP (OSBP) ≥160 mmHg and estimated glomerular filtration rate (eGFR) ≥45 mL/min per 1.73 m<sup>2</sup>, Group B, OSBP ≥140-159 mmHg and eGFR ≥45 mL/min per 1.73 m<sup>2</sup> and Group C, OSBP ≥140 mmHg and eGFR ≥15 mL/min per 1.73 m<sup>2</sup>. For all three groups subjects were required to be on at least 3 anti-hypertensive medications (including 1 diuretic), or to have documented drug intolerance such that they are unable to take 3 anti-hypertensive drugs. Responder analysis was also performed using a 5mmHg reduction in ambulatory systolic measurement to define responders.

**RESULTS** 133 patients from Group A (average age 61.6 ± 9.5 yrs taking on average 4.3 ± 2.3 anti-hypertensive medications) were included. Bilateral renal nerve ablation was performed using a percutaneous femoral approach. Baseline average OSBP was 181.9 ± 16 mmHg, average office diastolic BP (ODBP) was 97.8 ± 15.9 mmHg, average 24hr ambulatory SBP (ASBP) was 159.4 ± 17 mmHg, and average 24hr ambulatory DBP (ADBP) was 88.7 ± 12.9 mmHg. At present, 119 6-month and 88 12-month follow-up visits are completed. The average reduction in OSBP/ODBP was 18.5/8.4 mmHg and 18.2/9.5 mmHg at 6- and 12-month follow up respectively (p<0.0001 for all). The average reduction in ASBP/ADBP was 7.1/3.8 mmHg (p<0.0001 for both) and 9.8/4.2 mmHg (p<0.001 for both) at 6 and 12M follow up respectively. Neither eGFR nor serum creatinine changed significantly from baseline at either 6 or 12-months follow up. The following baseline factors were associated with the responder group at the 90% confidence level: younger age, less sleep apnea, higher eGFR, lower serum creatinine, higher systolic & diastolic ambulatory pressures.

**CONCLUSIONS** In this real world, post-marketing study we demonstrate that multi-electrode renal denervation results in durable, highly significant and safe lowering of both office BP and ambulatory BP parameters in patients with severe uncontrolled hypertension up to 12 months following treatment.

**CATEGORIES ENDOVASCULAR:** Hypertension Therapies and Renal Denervation

**KEYWORDS** Renal Denervation, Resistant hypertension

#### TCT-86

##### **Safety and Performance of the Next Generation EnligHTN™ Renal Denervation System in Patients with Drug-resistant Hypertension: 24-Month Results From a First-in-Human Multicentre Study**

Stephen G. Worthley,<sup>1</sup> Gerry T. Wilkins,<sup>2</sup> Mark W. Webster,<sup>3</sup> Joseph Montarello,<sup>4</sup> Paul Antonis,<sup>5</sup> Robert J. Whitbourn,<sup>6</sup> Roderic Warren<sup>7</sup>

<sup>1</sup>The University of Adelaide, Adelaide, Australia; <sup>2</sup>Dunedin Hospital, Dunedin, New Zealand; <sup>3</sup>Auckland City Hospital, Auckland, New Zealand; <sup>4</sup>Royal Adelaide Hospital, Adelaide, Australia; <sup>5</sup>Monash Heart, Melbourne, Australia; <sup>6</sup>Cardiovascular Research Centre, St. Vincent Hospital Melbourne, Melbourne, Victoria; <sup>7</sup>Royal Melbourne Hospital, Melbourne, Australia

**BACKGROUND** Catheter-based renal artery denervation therapy has become established as a therapeutic option in patients with resistant hypertension. We further investigated the safety and performance of the next generation EnligHTN™ Renal Denervation System (St. Jude Medical) in patients with drug-resistant hypertension.

**METHODS** The EnligHTN™ Renal Artery Ablation Catheter has 4 electrodes attached on a basket mounted at the tip of the catheter. The basket is collapsed and can be expanded via an external mechanism once the catheter is placed in the desired location of the renal artery. The next generation EnligHTN™ RF Ablation Generator utilizes a novel algorithm for the delivery of 1 minute of radio-frequency energy, optimized for simultaneous delivery of therapy through all 4 electrodes, with an interactive, intuitive user interface. Renal denervation was performed on 39 patients across 6 centers meeting the following inclusion criteria: 18-80 years of age, a systolic BP  $\geq 160$  mmHg, an average daytime systolic ambulatory BP  $\geq 135$  mmHg, on three or more antihypertensive agents (including a diuretic), and renal artery diameter  $\geq 4$  mm and length  $\geq 20$  mm. The primary endpoints are 1) to characterize the rate of serious procedural and device related adverse events from date of procedure through 6 months post procedure and 2) the change in office BP at 6 months post procedure. The secondary endpoints include the changes in 24 hour ambulatory BP and the characterization of renovascular safety and renal function change over time from baseline. Renal artery CT angiography was repeated at 6 months in all patients. The multi-electrode ablation catheter was introduced into each renal artery and two sets of denervation therapy delivered per renal artery.

**RESULTS** To date 37/38 patients have completed 18-months of follow-up post procedure. One serious device or procedure related adverse event, a pseudo aneurysm, has been observed as adjudicated by an independent Clinical Events Committee. There were no clinically significant changes in renal function through 18-months as observed in eGFR, serum creatinine, cystatin C, or urine albumin-to-creatinine ratio. 18-month office (and 12M, 24 hour ambulatory) BP reductions from baseline were -25/-8 (-11/-4) mmHg, which were statistically significant except for the ambulatory diastolic reduction. Renal artery denervation procedures were performed successfully in all patients, with an average of 4.33 ablation sets and 15.85 ablations performed per patient. The mean total ablation catheter insertion-to-removal time was 22.38 min and mean ablation time was 4.33 min per patient.

**CONCLUSIONS** Accumulated 24-month results from all sites will be presented at the meeting. After 18-months follow-up post procedure in this first-in-human study, we conclude that data demonstrates the next generation EnligHTN Renal Denervation System continues to be safe, rapid, and effective in the treatment of patients with drug-resistant, uncontrolled hypertension.

**CATEGORIES ENDOVASCULAR:** Hypertension Therapies and Renal Denervation

**KEYWORDS** Hypertension, Renal Denervation

#### TCT-87

##### **Non-invasive Renal Denervation Study Using Externally Delivered Focused Ultrasound in Severe Resistant Hypertension: 1 Year Follow up Results**

Roland E. Schmieder,<sup>1</sup> John A. Ormiston,<sup>2</sup> Petr Neuzil,<sup>3</sup> Zdenek Starek,<sup>4</sup> Patrick Kay,<sup>5</sup> Omar Dawood,<sup>6</sup> Thomas Anderson,<sup>6</sup> Michael Gertner,<sup>7</sup> William B. White<sup>8</sup>

<sup>1</sup>University Hospital Erlangen-Nürnberg, Erlangen, Germany; <sup>2</sup>Professor, University of Auckland Medical School, Auckland, New Zealand; <sup>3</sup>Homolce Hospital, Prague, Czech Republic; <sup>4</sup>St. Anne's University Hospital, Brno, Czech Republic; <sup>5</sup>Mercy Hospital, Auckland, New Zealand; <sup>6</sup>Kona Medical, Inc., Bellevue, WA; <sup>7</sup>Kona Medical, Inc, Bellevue, WA; <sup>8</sup>University of Connecticut School of Medicine, Farmington, CT

**BACKGROUND** The Kona Medical Surround Sound™ System is a non-invasive device for renal denervation that delivers externally focused ultrasound to the renal nerves using Doppler-based image guidance to track and correct for renal artery motion during the procedure. Aims: To evaluate the safety and efficacy of an entirely non-invasive approach to renal denervation using externally delivered focused ultrasound with real time Doppler-based image guidance in treatment resistant hypertension (TRH).

**METHODS** In 3 consecutive studies 69 patients with severe TRH, defined as persistent systolic blood pressure (BP)  $> 160$  mmHg despite 3 or more antihypertensive medications, were treated non-invasively with the Kona Medical Surround Sound System™. Focused ultrasound energy was delivered to the renal arteries bilaterally and surrounding tissue using Doppler-based imaging and continuous tracking with automatic correction for kidney motion throughout treatment. Patients received conscious sedation during the treatment period.

**RESULTS** At this time, all patients have completed 24 weeks follow-up and 61 patients have completed 52 weeks of follow-up. Post-denervation, the mean changes from baseline BP were -16.2/-6.7 mmHg at 3 weeks, -22.3/-9.0 mmHg at 6 weeks, -24.4/-9.9 mmHg at 12 weeks, -24.6/-9.0 mmHg at 24 weeks and -22.9/-9.9 mmHg 52 weeks. Response rates (drop in BP by  $> 10$  mmHg) was 75% at 6 and 12 months. No serious intervention related events have been reported to date. Forty-six percent of subjects (32/69) reported mild back pain immediately following the denervation treatment. The majority of cases (19/32) completely resolved within seven days post treatment and no case was associated with any motor, sensory deficits.

**CONCLUSIONS** This is the first data in humans using a non-invasive renal denervation system in severe TRH. Results showed clinically meaningful reductions in office BP through 52 weeks post-denervation. The procedure was well-tolerated with no serious adverse events. Sham-operator controlled studies with the Kona systems to evaluate the safety and efficacy of this novel non-invasive treatment are in the recruiting and planning stages.

**CATEGORIES ENDOVASCULAR:** Hypertension Therapies and Renal Denervation

**KEYWORDS** Hypertension, Renal Denervation, Ultrasound

#### TCT-88

##### **Transcatheter Perivascular Chemical Neurolysis to Produce Renal Denervation: Targeted, Local Delivery of Alcohol as a Viable Alternative to Radiofrequency Approaches**

Tim Fischell,<sup>1</sup> Felix Vega,<sup>2</sup> Darrin J. Kent,<sup>3</sup> Stefan C. Bertog,<sup>4</sup> Narayan Raju,<sup>5</sup> Elena Ladich,<sup>6</sup> Kazuyuki Yahagi,<sup>7</sup> Renu Virmani,<sup>8</sup> Vartan E. Ghazarian<sup>9</sup>

<sup>1</sup>Michigan State University, Kalamazoo, MI; <sup>2</sup>Preclinical Consultation, San Francisco, CA; <sup>3</sup>Rev1 Engineering, Murrieta, CA; <sup>4</sup>CardioVascular Center Frankfurt, Minneapolis, United States; <sup>5</sup>Pathology Research Associates, Hayward, CA; <sup>6</sup>CV Path, Gaithersburg, USA; <sup>7</sup>CVPath Institute, Inc., Gaithersburg, MD; <sup>8</sup>CVPath Institute, Inc., Gaithersburg, United States; <sup>9</sup>Ablative Solutions, Inc., Menlo Park, CA

**BACKGROUND** Despite recent setbacks and limitations with radio-frequency (RF)-based therapies, there is continued interest in renal denervation as a therapy for uncontrolled hypertension. We present an update of targeted "chemical renal denervation" using alcohol as the neurolytic agent, as an alternative method for renal denervation.

**METHODS** The Peregrine System™ is a novel endovascular catheter with three micro-needles which are deployed into the perivascular